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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/505,898	02/17/2000	Kirti Dave	065733/2262	7146

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EXAMINER	
WINKLER, ULRIKE	

ART UNIT	PAPER NUMBER
1648	

DATE MAILED: 03/13/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/505,898	DAVE ET AL.	
	Examiner	Art Unit	
	Ulrike Winkler	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 December 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *44-54 and 56-117* is/are pending in the application.

4a) Of the above claim(s) *48-53, 57-59, 66-71, 82-87, 93-105, 108-115* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *44-47,54-56,60-65,72-81,88-92,106,107,116 and 117* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

The amendment filed December 22, 2005 in response to the Office action of August 23, 2005 is acknowledged and has been entered. Claims 116-117 have been added. Claims 44-47, 54-56, 60-65, 72-81, 88-92, 106, 107 and newly added claims 116 and 117 are pending and are currently being examined.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office Action.

Claim Rejections - 35 USC § 103

The rejection of claims 44-46, 54, 56, 60-65, 72-81, 88-92, 106, 107 and newly added claims 116 and 117 under 35 U.S.C. 103(a) over Oprandy et al. (Journal of Clinical Microbiology, 1990, see IDS #5), Huang et al. (U.S.Pat. No. 5,712,172), WHO Bulletin (Bulletin of the World Health Organization, 1996, see IDS #5), Snowden et al. (Journal of Immunological Methods, 1991, see IDS #5), Pawlak et al. (U.S. Pat. No. 5,770,460), Hildreth et al. (Journal of Clinical Microbiology, 1982) and Collins et al. (American Journal of Tropical Medicine and Hygiene, 1984, see IDS) **is maintained for reasons of record.** The reference of Collins et al. has now been cited because the amended claims require the use of a field collected arthropod sample.

Applicants have amended the instant claims to require that the arthropod sample be a "field collected" arthropod sample and that the non-ionic detergent is "at a concentration of at least 0.1%."

Applicant's arguments are that neither the Oprandy nor the Hildreth reference teach an extraction solution that uses a non-ionic detergent and neither reference teaches the adequacy of the disclosed reagents for testing "field collected, blood engorged arthropods" or the use of "non-ionic detergent." The argument that the detergent must be present in the arthropod grinding process in order to expose at least one analyte is not convincing. The use of a non-ionic detergent in the grinding process to expose at least one analyte is within the skill of the ordinary artisan. The ordinary artisan upon reading the prior art would know that the presence or absence of a detergent in the arthropod grinding process is not critical to expose at least one analyte.

Oprandy teaches that the analyte in an arthropod vector can be detected using an ionic detergent (SDS). Hildreth et al. teaches that the absence of a detergent is not detrimental to the analyte detection assay using an arthropod sample. Collins et al. (cited in this rejection) teaches that analyte can be detected from an arthropod sample that has been collected in the field and ground up in the presence of a non-ionic detergent. From reading the references the ordinary artisan would determine that the presence or absence of a detergent, ionic or non-ionic, is not critical for the detection of an analyte (antigen) in a mosquito sample. The ordinary artisan would also determine after reading the references that the source of the mosquito is not critical for the success of the assay, field collected or laboratory raised mosquitoes both produce good results with the art known antibodies. Thus, the limitation on which Applicants' base their argument are shown in the art not to be critical for the function of the assay. The critical interaction for the detection of the analyte in the arthropod sample is between the antibody-antigen. So long as the antigen is not denatured or degraded and the antigen is solubilized (is found in the liquid portion) from the source an assay using a known antibody will predictably

interact with the antigen. Optimizing experimental conditions, including the timing of adding or not adding a detergent during the homogenization process, falls within the skills of an ordinary artisan. If the timing of adding the modulating compound produces an unexpected result, applicant needs to point out what the unexpected results are. Generally, differences in concentration or timing will not support the patentability of subject matter encompassed by the prior art unless there is evidence indicating such concentration or timing is critical. "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." *In re Aller*, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955). In this instance neither the source of the arthropod sample nor the presence of the non-ionic detergent in the grinding process is critical for the purpose of extracting an antigen from the arthropod sample.

Applicant's arguments and the Office's response are essentially the same as those of record. In response to Applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). Applicants arguments and the Offices response are essentially the same of record. Applicants' arguments are that none of the references are anticipatory. Applicants argue that the present invention has a wide application and makes use of a format that is more applicable to commercial production for field-collected samples.

In response to applicant's argument that there is no suggestion to combine the references, the examiner recognizes that obviousness can only be established by combining or modifying the

teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988)and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992).

In this instant applicants are claiming a method of detecting an analyte. The analyte detection depends on the specific interaction between the antibody and the analyte. The art recognizes that it is the antibody/analyte interaction that provides the means for the actual detecting property. The art also recognizes that regardless of the format of the assay that is used, the assay is dependent on the antibody/analyte interaction.

The instant invention is drawn to a method of analyzing an arthropod sample for an agent that may cause disease in mammals.

The method (claim 44) comprising the following steps:

(a) obtaining the filed collected arthropod sample,

(b) grinding the sample with buffered saline solution and a non-ionic detergent at a concentration of at least 0.1% to expose at least one analyte from the arthropod,

(c) contacting the liquid permeable support which contains a capture reagent with the sample from the previous step,

(d) allowing liquid to flow through the support by capillary action,

(e) detecting the presence of the analyte, and

(f) using a plurality of detectable analyte specific reagents for detecting arthropod carried agents.

The dependent claims contain the following additional limitations: the detection moiety, the placement of the analyte specific reagent, the arthropod is a mosquito, the liquid permeable support contains a control area, the analyte specific reagents are monoclonal antibodies, or gold and latex labeled antibodies, the non-ionic detergent is selected form NP-40, Tween-20 or Triton X-100, and the detergent concentration is greater than 0.1% and up to about 0.5%.

Applicants arguments are directed to point (b)/(c) of the method steps. Applicants' arguments are that the prior art samples always contain an additional step to clarify the arthropod sample before applying the method steps. The independent claims 44, 63 and 79 all utilize the transitional term comprising. MPEP 2111.03 The transitional term "comprising", which is synonymous with "including," "containing," or "characterized by," is inclusive or open-ended and does not exclude additional, unrecited elements or method steps. See, e.g., *Genentech, Inc. v. Chiron Corp.*, 112 F.3d 495, 501, 42 USPQ2d 1608, 1613 (Fed. Cir. 1997) ("Comprising" is a term of art used in claim language which means that the named elements are essential, but other elements may be added and still form a construct within the scope of the claim.) In this instance the additional clarification step taught in the prior art would fall within the meaning of the claim. Even if the claim limitation were to exclude a clarification step the use of non-purified samples is contemplated in the prior art. "The sample receiving zone may further serve to remove debris or interfering substances from the sample by physical entrapment without impeding the non-bibulous lateral flow" (see U.S. Pat # 5,770,460 column 2, lines 55-59).

The significance of the teaching of each of the prior references are as follows:

Collins et al. teaches collecting mosquitoes in the field. The mosquitoes are collected "from the walls, ceilings, and most productively from within the bed nets of native huts" in

Gambia (see page 539, column 1, paragraph 1). The collected mosquitoes were dried and later analyzed for *P. falciperum* sporozoite antigens. "To each microfuge tube containing a single dried mosquito was added 30 ul of phosphate buffered saline containing 1% bovine serum albumin (PBS/BSA) , 25 ug/ml of the protease inhibitor leupeptin and antipain, 1.7 units/ml aprotinin and 0.5% NP-40. This mixture was incubated for 1 hour, triturated (to pulverize and comminute thoroughly by rubbing and grinding) by hand with a flame sealed Pasteur pipette, then diluted with 300 ul PBS/BSA" (see page 539, paragraph spanning column 1-2). Antibodies in immunoradiometric assay then detected the sporozoite antigen. Field collected arthropod samples are treated with a non-ionic detergent before detecting the antigen. The reference does not teach using a dipstick assay to detect the antigen.

Oprandy et al. teaches using a mosquito for the purpose of detecting a malarial antigen when absorbed onto a solid membrane. The reference teaches exposing analytes by homogenizing the arthropod in a buffer containing SDS (an ionic detergent). Thus at the time the invention was made the ordinary artisan was aware that mosquito could be tested for the presence of malarial antigen in the insect vector itself. The detection is dependent on the antibody antigen interaction. The reference established that a mosquito could be tested for the presence of an agent that causes disease in a mammal. The reference is applicable because some of the dependent claims specifically look to detecting malarial antigen in the mosquito.

Hildreth et al. teach the public health surveillance of arboviruses typically involve, detecting human infection and infection in the mosquito vector population itself. The risk for human infection increases with the increase in the number of mosquitoes carrying the virus. Mosquitoes were ground up in saline supplemented with fetal bovine serum (a polypeptide

component), penicillin (an antimicrobial component) and streptomycin (an antimicrobial component) (see page 880, column 1, 2nd paragraph). The mosquito pools are diluted in a buffer containing 0.1% Tween 20, in saline with heat inactivated serum before adding to the ELISA plate, this would allow for the exposure of the antigen present in the mosquito pool. Thus the antibody/analyte interaction occurs in the presence of non-ionic detergent. The effectiveness of the procedure is dependent on the antibody/analyte interaction. The reference teaches that at the time the invention was made the ordinary artisan was aware that adding inhibitors and adding a polypeptide component adds to the stability of the sample to be tested.

Snowden et al. teaches a dipstick assay that combines the concepts of a double antibody sandwich ELISA, dot blotting and colloidal particle linked antibodies to produce a dipstick for multiple antigen detection. Without the antibody/analyte interaction the dipstick would not function. The dipstick used antibodies that were known to interact with an antigen. The reference teaches that known antigen/analyte interactions can be easily transformed into different assay formats without losing the critical antibody analyte interaction, which is necessary for the detection. Here capture antibodies where linked to the dipstick (made up of nitrocellulose membrane). After attaching the capture reagent the remaining binding sites were blocked. The dipstick was then placed an analyte containing liquid. After the interaction with the analyte the dipstick is placed into an analyte detecting reagent made up of an antibody linked to a dye. The dipstick is then analyzed for color development. The reference has immediate applicability to identify insect blood meals. The reference provides the motivation that the same technique can be applied for qualitative antigen (analyte) detection test for mammal diseases carried by the mosquito (see page 58, column 1, last paragraph).

WHO reference teaches that a dipstick assay can be used to detect malarial analyte in a blood sample from patient. The steps involved in the WHO reference are similar to the method taught by Snowden et al. above. Here there is a dipstick with a capture antibody, which is exposed to a liquid containing an analyte, the dipstick is incubated with detecting agent an analyzed for a positive reaction. The assay is dependent on the antibody/antigen interaction. The ordinary artisan is aware that the malarial parasite has different epitopes (analyte) exposed during different life stages of the parasite. Thus, to assay a mosquito for the presence of a malarial antigen would require the use of an antibody that recognizes a mosquito stage analyte (antigen) of malaria, such as the one taught by Oprandy et al.

Huang et al. teaches a lateral flow device comprising a sample receiving area, an analyte detection area made up of mobile labeling areas followed by a capture reagent area. The analyte detection area sits between the sample receiving area and the end flow region. The method of detection using the device depends on the antibody/analyte interaction of interest and can be modified accordingly (see column 1, lines 45-49).

Pawlak et al. teaches a similar later flow device to that of Huang et al. above. The device comprises a sample receiving zone, a labeling zone, a capture zone and an absorbent end zone. The reference teaches that the sample receiving zone can serve to remove debris or interfering substance by physical entrapment without impeding nonbibulous lateral flow. Thus the reference teaches that the sample may contain debris and the sample does not need to be clarified before using device. The method of detection using the device depends on the antibody/analyte interaction of interest and can be modified accordingly.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to utilize the analyte detection reagents as taught by Collins et al., Oprandy et al. and/or Hildreth et al. and apply them to the device taught by Huang et al., Pawlak et al., WHO bulletin and Snowden et al. One having ordinary skill in the art would recognize that the methods of detection using the various devices are dependent on the antibody/analyte interaction and are not dependent the particulars of the device to carry out the detection step.

One having ordinary skill in the art would have been motivated to move from an ELISA based assay system, or a Western blotting system, or an immunoradiometric assay to a dipstick or lateral flow device for the ease of using the assay by unskilled personal. The ordinary artisan at the time the invention was filed was well aware that in order to determine the risk of arthropod-vector disease spread it is necessary to survey the insect population for these etiologic agent (as taught by Hildreth et al.). This information is important to assess the efficacy of insect control and abatement programs.

One having ordinary skill in the art would have a high expectation of success in applying the antibodies and the methods of exposing the analyte using detergents as taught by Collins et al., Oprandy et al. and/or Hildreth et al. and formulate them into the device as taught by Huang et al., the WHO Bulletin and Snowden et al. teaches that an Snowden et al. clearly teaches that reagents used for an ELISA based test are predictably adaptable to the dipstick protocol. In the experiments comparing blood meal analysis of mosquito using the dipstick assay and ELISA showed 100% agreement and 100% accuracy (see Snowden et al., page 58, last paragraph). Therefore, the instant invention is obvious over the cited references.

The rejection of claims 44-47, 54, 56, 60-65, 72-81, 88-92, 106, 107 and newly added claims 116 and 117 under 35 U.S.C. 103(a) as being unpatentable over Oprandy et al. (Journal of Clinical Microbiology, 1990, from applicant's IDS), Huang et al. (U.S.Pat. No. 5,712,172), WHO Bulletin (Bulletin of the World Health Organization, 1996, see IDS #5) and Snowden et al. (Journal of Immunological Methods, 1991, see IDS #5), Pawlak et al. (U.S. Pat. No. 5,770,460), Hildreth eta l. (Journal of Clinical Microbiology, 1982) and Collins et al. (American Journal of Tropical Medicine and Hygiene, 1984, see IDS) in view of Rattanarithikuln et al. (American Journal of Tropical Medicine, 1996, from applicant's IDS) and Sithiprasasna et al. (Annals of Tropical Medicine and Parasitology, from applicant's IDS) **is maintained** for reason of record. The reference of Collins et al. has now been cited because the amended claims require the use of a field collected arthropod sample.

Applicant's arguments and the Office's response are essentially the same as those set out in the above rejection. Applicant further argues that neither Rattanarithikuln et al. or Sithiprasasna et al. teach or motivate the selection of monoclonal antibodies for the detection of arthropod-borne disease vectors. This is not found convincing because Rattanarithikuln et al. teach using monoclonal antibodies in ELISA detection assay (see page 116, 3rd paragraph). Sithiprasasna et al. teach using monoclonal antibodies for the detection of Dengue virus, a flavivirus (see page 399, column 1). The panel assay does not provide a contribution over the prior art. It is obvious from the prior art that Rattanarithikuln et al. used two different monoclonal antibodies in an ELISA assay to differentiate whether the misquotes carries the *P. vivax* or the *P. falciparum* malarial parasite. Merely changing the format of an assay (vertical v. horizontal or PVDF v. nitrocellulose) that depends on the same unique interaction between an

antibody and the analyte (antigen) for its function does not distinguish the instant invention over the prior art. Snowden et al. clearly teaches that reagents used for an ELISA based test are predictably adaptable to the dipstick protocol. In the experiments comparing blood meal analysis of mosquito using the dipstick assay and ELISA showed 100% agreement and 100% accuracy (see Snowden et al., page 58, last paragraph). Snowden et al. also teaches that the dipstick assay has the advantage that two or more antigens may be tested at the same time, indicating the efficiency of the assay method. Therefore, the instant invention is obvious over the prior art.

Conclusion

No claims allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG (November 15, 1989). The Group 1600 Official Fax number is: (571) 273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Tech Center representative whose telephone number is (571)-272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR

system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ulrike Winkler, Ph.D. whose telephone number is 571-272-0912. The examiner can normally be reached M-F, 8:30 am - 5 pm. The examiner can also be reached via email [ulrike.winkler@uspto.gov].

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel, can be reached at 571-272-0902.

ULRIKE WINKLER, PH.D.
PRIMARY EXAMINER

3/6/05